HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Pharmacovigilance updates and the signal management process

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Reminder- Good Pharmacovigilance Practice

- A series of 5 modules (VGVP) relating to good PhV practice are available on the EMA website
  - Signal management
  - Controls and pharmacovigilance inspections
  - Pharmacovigilance systems, their quality management systems and pharmacovigilance system master files
  - Collection and recording of suspected adverse events for veterinary medicinal products
  - Veterinary pharmacovigilance communication
- These 5 modules have replaced Volume 9B

Reminder

- ✘ The Detailed Description of the Pharmacovigilance System (DDPS) is no longer required.
- ✓ The MAH is now required to have a Pharmacovigilance System Master File in place
- ✘ No longer a requirement to assign a causality to adverse event reports (ABON)
- ✓ The MAH is required to conduct a continuous signal management process which has replaced Periodic Safety Update Reports (PSURs)

Reminders- the QPPV is…

- Responsible for elaborating and maintaining the Pharmacovigilance System Master File (PSMF)
- Responsible for allocating a reference number to the PSMF and communicating that number to the Union PhV database for each product
- Responsible for recording **all** types of adverse event reports in the Union PhV database within **30** calendar days of receipt
- Responsible for applying the signal management process

Signal management process

- We have moved to signal management!
- Training can be found on the EMA website here: https://www.ema.europa.eu/en/events/union-pharmacovigilance-database-follow-webinar-signal-detection-evaluation-yearly-reporting

What is required of MAH's when it comes to signal management?

- Continuous monitoring of the benefit-risk balance of a veterinary medicinal product.
- MAHs are required to record at least **annually** all results and outcomes of the signal management process in the Union PhV database.
  - ✓ Signals which require reporting without delay.
  - ✓ Any signals validated and assessed throughout the year
  - ✓ Annual statement
- Signal management process elaborated further in the Implementing Regulation on GPP and in particular in the VGVP signal management.

Signals which require reporting without delay

- ESI (emerging safety issue)- entered into the relevant module on the Union PhV Database (IRIS), description of issue and proposed actions, no later than 3 **working** days.
- Other confirmed signals requiring potential regulatory action- entered into the signal module (IRIS), no later than 30 **calendar** days
- Data entered- Administrative info, one entry per signal, specifying species, VeDDRA preferred term/type of AE, **cumulative number of cases**, rationale, results and conclusion
- Following a risk-based approach, as a simple rule, a minimum of 3 case reports are needed for signals concerning Medically Important (MI) terms and 5 case reports for signals involving any other VeDDRA terms.

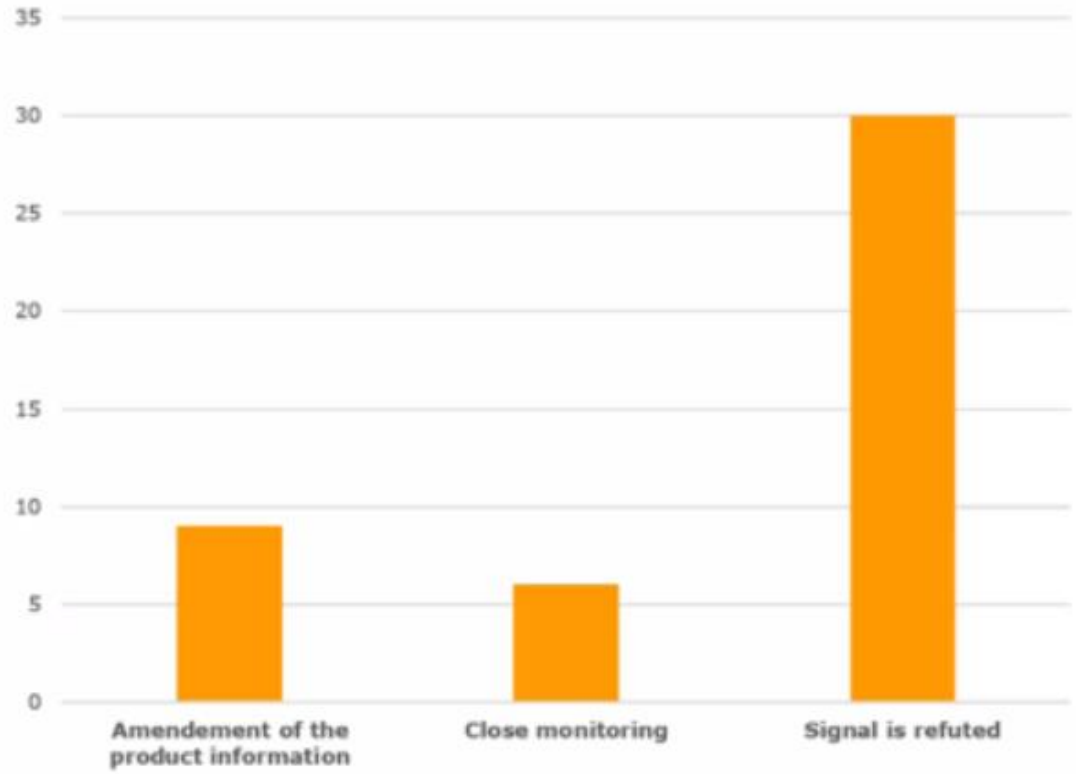
Annual Statement

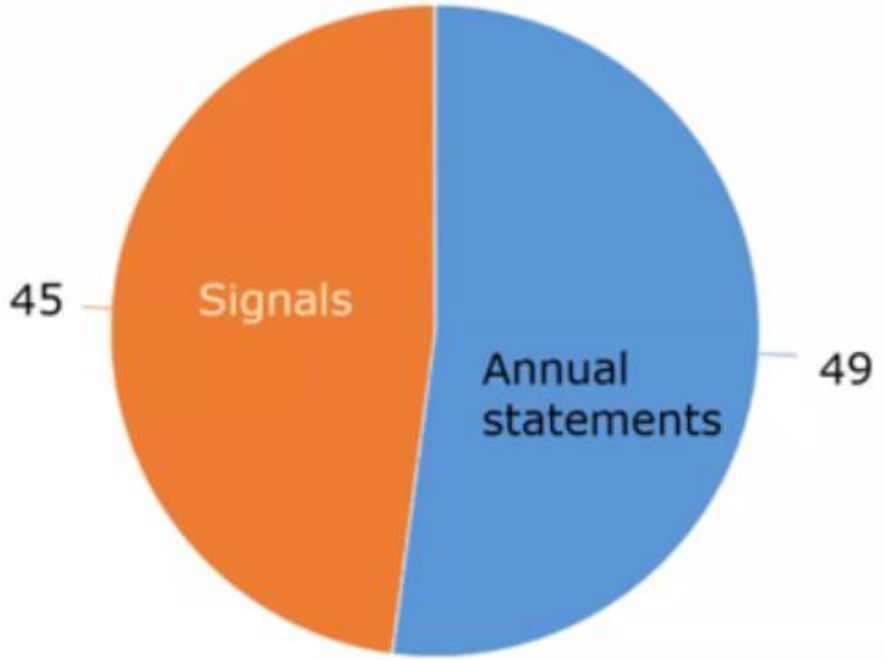
- Due dates (DLPs) for recording outcome of the signal management process including a conclusion on the B/R balance have been set for CAPs. Work still underway regarding Non-CAPs
- Record results and outcomes of the signal management process in the Union PhV Database
- All validated and assessed signals throughout the year with no proposals for further regulatory actions by the MAH to be submitted **by the due date** of the annual statement
- Record a conclusion on the B/R balance for each of their products in the Union PhV Database and confirm that the process has been conducted

IRIS

- All validated and assessed signals and annual statements should be submitted via IRIS
- iris-guide-applicants-how-create-submit-scientific-applications-industry-individual-applicants_en.pdf (europa.eu) (user manual)
- P-SMEG are currently developing a Processes description document that will be published in due course

Signals and Annual Statements submitted to IRIS between 28 Jan and 12 May





Signal management entry

- When submitting a signal to IRIS MAH's are requested to complete the 'Veterinary Signal Assessment Report' template which can be found on the EMA website:

  Pharmacovigilance (veterinary medicines) | European Medicines Agency (europa.eu)

Pilot Signal Management Expert Group (P-SMEG)

- Role:
  - Set up and test the new process regarding signal management of adverse reactions to veterinary medicinal products in the European Union,
  - To identify, prioritise and assess safety issues that must be addressed in relation to the monitoring activities,
  - To support/perform targeted signal management activities across the network,
  - To transmit to the Pharmacovigilance Working Party signals detected and proposed regulatory actions,
  - To contribute to the preparation and provision of training for national competent authorities (NCAs) and stakeholders
  - Evaluate annual statements and statements that the signal management procedure has been conducted and all assessed signals have been detected
- The group is a worksharing group composed of delegates from both the EMA and NCAs, including the HPRA, who meet weekly at present.

Signal management process

- Signal validation
  - Temporal association, not based only on duplicate reports, not already reflected in the PI adequately
- Further assessment- **cumulative review**
  - Number of cases, incidence, additional cases, quality of data
- MAH to conclude if available evidence reviewed supports a potential causal association, or not.

Recommendation for action by the MAH

- Casual association supported, change in B/R balance
  - ESI (emerging safety issue)- notify within 3 working days
  - Otherwise notify within 30 calendar days
  - Propose other actions and risk minimisation measures
- Potential cause unlikely
  - Signal refuted, no further action
- Information insufficient
  - Close monitoring (report at each yearly due date)
  - PASS (voluntarily by MAH/requested by the Agency or NCA (Art. 76 (3) and (4))

Common Issues/Questions

- The PSMF summary does not need to be included in the dossier for existing products. Updates to the PSMF summary shall be handled via VNRA by MAHs; at that point, they will be reflected in the dossier.
- For existing products it has been agreed that a VNRA C.6 should be submitted by the MAH to provide information on the PSMF reference number and location
- The UPD fields on QPPV name and location contain placeholder data which MAHs can update only via variation not requiring assessment
- **MAHs have been asked to hold off submitting certain VNRAs until June/July when the release of further VNRA functionality will go live**

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Adverse event reports

- MAHs are kindly reminded when submitting Adverse event reports to EVVET3 that as much information as possible is provided
- It is important to retain the quality of the data within the Union Pharmacovigilance database
- Updated version of the EVVet3 BPG is due to be published by the EMA very soon.

Useful Guidance

- HPRA website including Q&A document, information from the Vet info day that took place in Oct 2021
- EMA website: https://www.ema.europa.eu/en/veterinary-regulatory/post-authorisation/pharmacovigilance-veterinary-medicines including Q&A documents, recorded webinars

Further training will be provided by the EMA

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Thank you

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